

In order for a claimed invention to be obvious, the invention as a whole must be considered, and in particular every limitation of the claim must be disclosed or suggested by the prior art. This means that for the present claims, the cited publications must disclose or suggest a method of transplanting hematopoietic cells from a donor source into a genetically unrelated recipient comprising administering to the recipient, in combination with the administration of the hematopoietic cells, an amount of mononuclear cells which are treated so as to substantially reduce their ability to cause graft versus host disease while they retain their ability to proliferate in the recipient and facilitate engraftment of the hematopoietic cells in the recipient; and administering to the recipient an effective amount of hematopoietic cells. Applicants submit that the cited publications do not disclose or suggest all of these features.

The Examiner admits in the November 18, 2002, Office Action that U.S. Patent No. 5,800,539 does not teach that the treated T cells retain their ability to proliferate in the recipient. Thus, the rejection relies on Sykes et al. to teach this limitation. The Examiner alleges that Sykes et al. teaches that "for successful transplantation of hematopoietic cells from donor to recipient, it is essential that after treatment T cells are not completely depleted" and that Sykes et al. also teaches treatment with fludarabine. The Examiner then reaches the erroneous conclusion that "it would be obvious to one of ordinary skill in the art at the time the invention was made to **deduce** that said non-eliminated T cells would retain their ability to proliferate in the recipient"(emphasis added).

This is incorrect. While Sykes et al. does disclose that T cells should not be completely depleted, it cannot be assumed (and thus could not be deduced) that the remaining cells would retain the ability to proliferate nor that such a characteristic would be desirable. The presence or absence of T cells in the recipient is completely independent of their ability to proliferate. The art is replete with examples of non-proliferating T cells (see, for example, Jenkins MK, Schwartz, RH. (1987) *J. Exp Med.* 165:302-19; Jenkins MK, et al. (1987) *Proc Natl. Acad. Sci.* 84:5409-13; Quill H, Schwartz, RH. (1987) *J. Immunol.* 138:3704-12; abstracts of which are submitted with this Response). While Sykes et al. may indicate that the **presence** of some T

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cells is desirable, Sykes et al. does not indicate or suggest that **proliferation** of those T cells is required or desirable.

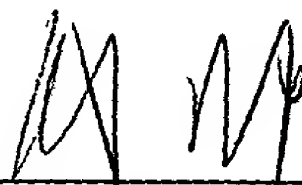
In fact, and to the contrary, Sykes et al. discloses that "in preferred embodiments, immune cell activity, e.g., T cell activity, preferably graft reactive T cell activity, is inhibited in the subject" (page 14, lines 26-31). By this, Sykes et al. means that the number of T cells are reduced. This is made clear where Sykes et al. defines the term "immune cell activity" as "reducing the **number** of active immune cells, e.g., thymocytes, T cells...in a subject. Inhibition can include partial inhibition or partial reduction (as opposed to total elimination) of the number of active immune cells, e.g., T cells" (page 10, lines 18-22; emphasis added). This definition emphasizes reduction in the number of cells, not in any change in cell characteristics. Thus, it is clear that Sykes et al. does not disclose or suggest that the T cells are able to proliferate. For at least these reasons, the combination of U.S. Patent No. 5,800,539 with Sykes et al. (WO 99/25367) does not make claims obvious.

Pursuant to the above remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

It is believed that no fee is due with this Response; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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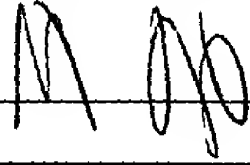
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I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on the date indicated below.

Robert A. Hodges



Date

2/12/2003